## SEOUENCE LISTING

<110> THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE GERMINO, Gregory WATNICK, Terry PHAKDEEKITCHAROEN, Bunyong

- <120> DETECTION AND TREATMENT OF POLYCYSTIC KIDNEY DISEASE
- <130> JHU1680-2
- <150> US 60/283,691
- <151> 2001-07-13
- <150> US 60/218,261
- 2000-07-13
- <160> 113
- <170> PatentIn version 3.0
- <210> 1
- <211> 53522
- <212> DNA
- <213> Homo sapiens

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<213> Homo sapiens

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Leu Trp Leu Gly Ala Leu Ala Gly Gly Pro Gly Arg Gly Cys Gly Pro
20 25 30

Cys Glu Pro Pro Cys Leu Cys Gly Pro Ala Pro Gly Ala Ala Cys Arg 35 40 45

Val Asn Cys Ser Gly Arg Gly Leu Arg Thr Leu Gly Pro Ala Leu Arg

|            | 50           |            |            |            |            | 55         |              |              |            |            | 60         |            |            |            |            |
|------------|--------------|------------|------------|------------|------------|------------|--------------|--------------|------------|------------|------------|------------|------------|------------|------------|
| Ile<br>65  | Pro          | Ala        | qaA        | Ala        | Thr<br>70  | Glu        | Leu          | Asp          | Val        | Ser<br>75  | His        | Asn        | Leu        | Leu        | Arg<br>80  |
| Ala        | Leu          | Asp        | Val        | Gly<br>85  | Leu        | Leu        | Ala          | Asn          | Leu<br>90  | Ser        | Ala        | Leu        | Ala        | Glu<br>95  | Leu        |
| Asp        | Ile          | Ser        | Asn<br>100 | Asn        | Lys        | Ile        | Ser          | Thr<br>105   | Leu        | Glu        | Glu        | Gly        | Ile<br>110 | Phe        | Ala        |
| Asn        | Leu          | Phe<br>115 | Asn        | Leu        | Ser        | Glu        | Ile<br>120   | Asn          | Leu        | Ser        | Gly        | Asn<br>125 | Pro        | Phe        | Glu        |
| Cys        | Asp<br>130   | Cys        | Gly        | Leu        | Ala        | Trp<br>135 | Leu          | Pro          | Gln        | Trp        | Ala<br>140 | Glu        | Glu        | Gln        | Gln        |
| Val<br>145 | Arg          | Val        | Val        | Gln        | Pro<br>150 | Glu        | Ala          | Ala          | Thr        | Cys<br>155 | Ala        | Gly        | Pro        | Gly        | Ser<br>160 |
| Leu        | Ala          | Gly        | Gln        | Pro<br>165 | Leu        | Leu        | Gly          | Ile          | Pro<br>170 | Leu        | Leu        | Asp        | Ser        | Gly<br>175 | Cys        |
| Gly        | Glu          | Glu        | Tyr<br>180 | Val        | Ala        | Cys        | Leu          | Pro<br>185   | Asp        | Asn        | Ser        | Ser        | Gly<br>190 | Thr        | Val        |
| Ala        | Ala          | Val<br>195 | Ser        | Phe        | Ser        | Ala        | Ala<br>200   | His          | Glu        | Gly        | Leu        | Leu<br>205 | Gln        | Pro        | Glu        |
| Ala        | Cys<br>210   | Ser        | Ala        | Phe        | Cys        | Phe<br>215 | Ser          | Thr          | Gly        | Gln        | Gly<br>220 | Leu        | Ala        | Ala        | Leu        |
| Ser<br>225 | Glu          | Gln        | Gly        | Trp        | Cys<br>230 | Leu        | Cys          | Gly          | Ala        | Ala<br>235 |            | Pro        | Ser        | Ser        | Ala<br>240 |
| Ser        | Phe          | Ala        | Cys        | Leu<br>245 |            | Leu        | Cys          | Ser          | Gly<br>250 |            | Pro        | Ala        | Pro        | Pro<br>255 | Ala        |
| Pro        | Thr          | Cys        | Arg<br>260 | Gly        | Pro        | Thr        | Leu          | Leu<br>265   |            | His        | Val        | Phe        | Pro<br>270 | Ala        | Ser        |
| Pro        | Gly          | Ala<br>275 |            | Leu        | . Val      | Gly        | Pro<br>280   | His          | Gly        | Pro        | Leu        | Ala<br>285 | Ser        | Gly        | Gln        |
| Leu        | . Ala<br>290 |            | Phe        | His        | Ile        | Ala<br>295 |              | Pro          | Leu        | ı Pro      | Val<br>300 |            | . Asp      | Thr        | Arg        |
| Trp<br>305 |              | Phe        | Gly        | Asp        | Gly<br>310 |            | Ala          | Gli          | ı Val      | Asp<br>315 |            | ı Ala      | Gly        | Pro        | 320        |
| Ala        | . Ser        | His        | Arg        | Tyr<br>325 |            | Lev        | ı Pro        | Gly          | 7 Arg      |            | f His      | val        | . Thr      | Ala<br>335 | val        |
| Leu        | ı Ala        | Leu        | Gly<br>340 |            | a Gly      | / Sei      | c Ala        | a Let<br>34! |            | ı Gly      | / Thi      | Asp        | 350        | Glr        | ı Val      |
| Glu        | ı Ala        | Ala<br>355 |            | ) Ala      | a Ala      | a Lei      | ı Glu<br>360 |              | ı Va       | l Cys      | s Pro      | Ser<br>365 |            | · Val      | l Gln      |

Ser Asp Glu Ser Leu Asp Leu Ser Ile Gln Asn Arg Gly Gly Ser Gly 370 375 380

Leu Glu Ala Ala Tyr Ser Ile Val Ala Leu Gly Glu Glu Pro Ala Arg 385 390 395 400

Ala Val His Pro Leu Cys Pro Ser Asp Thr Glu Ile Phe Pro Gly Asn 405 410 415

Gly His Cys Tyr Arg Leu Val Val Glu Lys Ala Ala Trp Leu Gln Ala 420 425 430

Gln Glu Gln Cys Gln Ala Trp Ala Gly Ala Ala Leu Ala Met Val Asp 435 440 445

Ser Pro Ala Val Gln Arg Phe Leu Val Ser Arg Val Thr Arg Ser Leu 450 455 460

Asp Val Trp Ile Gly Phe Ser Thr Val Gln Gly Val Glu Val Gly Pro 465 470 475 480

Ala Pro Gln Gly Glu Ala Phe Ser Leu Glu Ser Cys Gln Asn Trp Leu 485 490 495

Pro Gly Glu Pro His Pro Ala Thr Ala Glu His Cys Val Arg Leu Gly 500 505 510

Pro Thr Gly Trp Cys Asn Thr Asp Leu Cys Ser Ala Pro His Ser Tyr 515 520 525

Val Cys Glu Leu Gln Pro Gly Gly Pro Val Gln Asp Ala Glu Asn Leu 530 535 540

Leu Val Gly Ala Pro Ser Gly Asp Leu Gln Gly Pro Leu Thr Pro Leu 545 550 555 560

Ala Gln Gln Asp Gly Leu Ser Ala Pro His Glu Pro Val Glu Val Met 565 570 575

Val Phe Pro Gly Leu Arg Leu Ser Arg Glu Ala Phe Leu Thr Thr Ala 580 585 590

Glu Phe Gly Thr Gln Glu Leu Arg Arg Pro Ala Gln Leu Arg Leu Gln 595 600 605

Val Tyr Arg Leu Leu Ser Thr Ala Gly Thr Pro Glu Asn Gly Ser Glu 610 615 620

Pro Glu Ser Arg Ser Pro Asp Asn Arg Thr Gln Leu Ala Pro Ala Cys 625 630 635 640

Met Pro Gly Gly Arg Trp Cys Pro Gly Ala Asn Ile Cys Leu Pro Leu 645 650 655

Asp Ala Ser Cys His Pro Gln Ala Cys Ala Asn Gly Cys Thr Ser Gly
660 665 670

Pro Gly Leu Pro Gly Ala Pro Tyr Ala Leu Trp Arg Glu Phe Leu Phe 675 680 685

Ser Val Pro Ala Gly Pro Pro Ala Gln Tyr Ser Val Thr Leu His Gly 690 695 700

- Gln Asp Val Leu Met Leu Pro Gly Asp Leu Val Gly Leu Gln His Asp 705 710 715 720
- Ala Gly Pro Gly Ala Leu Leu His Cys Ser Pro Ala Pro Gly His Pro
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- Gly Pro Arg Ala Pro Tyr Leu Ser Ala Asn Ala Ser Ser Trp Leu Pro 740 745 750
- His Leu Pro Ala Gln Leu Glu Gly Thr Trp Gly Cys Pro Ala Cys Ala
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- Arg Pro Asn Pro Gly Leu Arg Leu Pro Gly Arg Tyr Glu Val Arg Ala
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- Lys Leu Ser Leu Thr Ala Ser Asn His Val Ser Asn Val Thr Val Asn 995 1000 1005
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- Val Ser Thr Val Pro Ala Val Leu Ser Pro Asn Ala Thr Leu Ala

|     | 1025        |     |       |       |       | 1030        |     |       |       | 1035 |             |     |       |       |
|-----|-------------|-----|-------|-------|-------|-------------|-----|-------|-------|------|-------------|-----|-------|-------|
|     | Thr<br>1040 | Ala | Gly   | Val   | Leu   | Val<br>1045 | Asp | Ser   | Ala   | Val  | Glu<br>1050 | Val | Ala   | Phe   |
|     | Trp<br>1055 | Thr | Phe   | Gly   | Asp   | Gly<br>1060 | Glu | Gln   | Ala   | Leu  | His<br>1065 | Gln | Phe   | Gln   |
|     | Pro<br>1070 | Tyr | Asn   | Glu   | Ser   | Phe<br>1075 | Pro | Val   | Pro   | Asp  | Pro<br>1080 | Ser | Val   | Ala   |
|     | Val<br>1085 | Leu | Val   | Glu   | His   | Asn<br>1090 | Val | Thr   | His   | Thr  | Tyr<br>1095 | Ala | Ala   | Pro   |
| Gly | Glu<br>1100 | Tyr | Leu   | Leu   | Thr   | Val<br>1105 | Leu | Ala   | Ser   | Asn  | Ala<br>1110 | Phe | Glu   | Asn   |
| Leu | Thr<br>1115 | Gln | Gln   | Val   | Pro   | Val<br>1120 | Ser | Val   | Arg   | Ala  | Ser<br>1125 | Leu | Pro   | Ser   |
| Val | Ala<br>1130 | Val | Gly   | Val   | Ser   | Asp<br>1135 | Gly | Val   | Leu   | Val  | Ala<br>1140 | Gly | Arg   | Pro   |
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| Tyr | Thr<br>1160 | _   | Asp   | Phe   | Gly   | Asp<br>1165 |     | Ser   | Pro   | Val  | Leu<br>1170 | Thr | Gln   | Ser   |
| Gln | Pro<br>1175 |     | Ala   | Asn   | His   | Thr<br>1180 |     | Ala   | Ser   | Arg  | Gly<br>1185 | Thr | Tyr   | His   |
| Val | Arg<br>1190 |     | Glu   | Val   | Asn   | Asn<br>1195 | Thr | Val   | Ser   | Gly  | Ala<br>1200 | Ala | Ala   | Gln   |
| Ala | Asp<br>1205 |     | Arg   | Val   | Phe   | Glu<br>1210 |     | Leu   | Arg   | Gly  | Leu<br>1215 |     | Val   | Asp   |
| Met | Ser<br>1220 |     | Ala   | Val   | Glu   | Gln<br>1225 |     | Ala   | Pro   | Val  | Val<br>1230 |     | Ser   | Ala   |
| Ala | Val<br>1235 |     | Thr   | Gly   | Asp   | Asn<br>1240 |     | Thr   | Trp   | Thr  | Phe<br>1245 |     | Met   | Gly   |
| Asp | Gly<br>1250 |     | Val   | Leu   | Ser   | Gly<br>1255 |     | Glu   | Ala   | Thr  | Val<br>1260 |     | His   | Val   |
| Tyr | Leu<br>1265 | _   | Ala   | Gln   | Asn   | Cys<br>1270 |     | Val   | Thr   | Val  | Gly<br>1275 |     | Gly   | Ser   |
| Pro | Ala<br>1280 |     | His   | . Leu | Ala   | Arg<br>1285 |     | Leu   | His   | Val  | Leu<br>1290 |     | . Phe | . Val |
| Leu | Glu<br>1295 |     | Lev   | ı Arg | y Val | Glu<br>1300 |     | Ala   | . Ala | Cys  | Ile<br>1305 |     | Thr   | Gln   |
| Pro | Asp<br>1310 |     | . Arg | g Leu | ı Thr | Ala<br>1315 |     | · Val | Thr   | Gly  | Asn<br>1320 |     | Ala   | a His |
| Tyr | Leu<br>1325 |     | e Asp | Trp   | Thr   | Phe 1330    |     | Asp   | Gly   | Ser  | Ser<br>1335 |     | ı Thr | Thr   |

- Val Arg Gly Cys Pro Thr Val Thr His Asn Phe Thr Arg Ser Gly 1340 1345 1350
- Thr Phe Pro Leu Ala Leu Val Leu Ser Ser Arg Val Asn Arg Ala 1355 1360 1365
- His Tyr Phe Thr Ser Ile Cys Val Glu Pro Glu Val Gly Asn Val 1370 1375 1380
- Thr Leu Gln Pro Glu Arg Gln Phe Val Gln Leu Gly Asp Glu Ala 1385 1390 1395
- Trp Leu Val Ala Cys Ala Trp Pro Pro Phe Pro Tyr Arg Tyr Thr 1400 1405 1410
- Trp Asp Phe Gly Thr Glu Glu Ala Ala Pro Thr Arg Ala Arg Gly 1415 1420 1425
- Pro Glu Val Thr Phe Ile Tyr Arg Asp Pro Gly Ser Tyr Leu Val 1430 1435 1440
- Thr Val Thr Ala Ser Asn Asn Ile Ser Ala Ala Asn Asp Ser Ala 1445 1450 1455
- Leu Val Glu Val Gln Glu Pro Val Leu Val Thr Ser Ile Lys Val 1460 1465 1470
- Asn Gly Ser Leu Gly Leu Glu Leu Gln Gln Pro Tyr Leu Phe Ser 1475 1480 1485
- Ala Val Gly Arg Gly Arg Pro Ala Ser Tyr Leu Trp Asp Leu Gly 1490 1495 1500
- Asp Gly Gly Trp Leu Glu Gly Pro Glu Val Thr His Ala Tyr Asn 1505 1510 1515
- Ser Thr Gly Asp Phe Thr Val Arg Val Ala Gly Trp Asn Glu Val 1520 1525 1530
- Ser Arg Ser Glu Ala Trp Leu Asn Val Thr Val Lys Arg Arg Val 1535 1540 1545
- Arg Gly Leu Val Val Asn Ala Ser Arg Thr Val Val Pro Leu Asn 1550 1560
- Gly Ser Val Ser Phe Ser Thr Ser Leu Glu Ala Gly Ser Asp Val 1565 1570 1575
- Arg Tyr Ser Trp Val Leu Cys Asp Arg Cys Thr Pro Ile Pro Gly 1580 1585 1590
- Gly Pro Thr Ile Ser Tyr Thr Phe Arg Ser Val Gly Thr Phe Asn 1595 1600 1605
- Ile Ile Val Thr Ala Glu Asn Glu Val Gly Ser Ala Gln Asp Ser 1610 1615 1620
- Ile Phe Val Tyr Val Leu Gln Leu Ile Glu Gly Leu Gln Val Val 1625 1630 1635

- Gly Gly Arg Tyr Phe Pro Thr Asn His Thr Val Gln Leu Gln 1640 1645 1650
- Ala Val Val Arg Asp Gly Thr Asn Val Ser Tyr Ser Trp Thr Ala 1655 1660 1665
- Trp Arg Asp Arg Gly Pro Ala Leu Ala Gly Ser Gly Lys Gly Phe 1670 1675 1680
- Ser Leu Thr Val Leu Glu Ala Gly Thr Tyr His Val Gln Leu Arg 1685 1690 1695
- Ala Thr Asn Met Leu Gly Ser Ala Trp Ala Asp Cys Thr Met Asp 1700 1705 1710
- Phe Val Glu Pro Val Gly Trp Leu Met Val Ala Ala Ser Pro Asn 1715 1720 1725
- Pro Ala Ala Val Asn Thr Ser Val Thr Leu Ser Ala Glu Leu Ala 1730 1735 1740
- Gly Gly Ser Gly Val Val Tyr Thr Trp Ser Leu Glu Glu Gly Leu 1745 1750 1755
- Ser Trp Glu Thr Ser Glu Pro Phe Thr Thr His Ser Phe Pro Thr 1760 1765 1770
- Pro Gly Leu His Leu Val Thr Met Thr Ala Gly Asn Pro Leu Gly 1775 1780 1785
- Ser Ala Asn Ala Thr Val Glu Val Asp Val Gln Val Pro Val Ser 1790 1795 1800
- Gly Leu Ser Ile Arg Ala Ser Glu Pro Gly Gly Ser Phe Val Ala 1805 1810 1815
- Ala Gly Ser Ser Val Pro Phe Trp Gly Gln Leu Ala Thr Gly Thr 1820 1825 1830
- Asn Val Ser Trp Cys Trp Ala Val Pro Gly Gly Ser Ser Lys Arg 1835 1840 1845
- Gly Pro His Val Thr Met Val Phe Pro Asp Ala Gly Thr Phe Ser 1850 1855 1860
- Ile Arg Leu Asn Ala Ser Asn Ala Val Ser Trp Val Ser Ala Thr 1865 1870 1875
- Tyr Asn Leu Thr Ala Glu Glu Pro Ile Val Gly Leu Val Leu Trp 1880 1885 1890
- Ala Ser Ser Lys Val Val Ala Pro Gly Gln Leu Val His Phe Gln 1895 1900 1905
- Ile Leu Leu Ala Ala Gly Ser Ala Val Thr Phe Arg Leu Gln Val 1910 1915 1920
- Gly Gly Ala Asn Pro Glu Val Leu Pro Gly Pro Arg Phe Ser His 1925 1930 1935
- Ser Phe Pro Arg Val Gly Asp His Val Val Ser Val Arg Gly Lys

|     | 1940        |     |     |     |       | 1945        |     |       |       |     | 1950        |     |       |     |
|-----|-------------|-----|-----|-----|-------|-------------|-----|-------|-------|-----|-------------|-----|-------|-----|
|     | His<br>1955 | Val | Ser | Trp | Ala   | Gln<br>1960 | Ala | Gln   | Val   | Arg | Ile<br>1965 | Val | Val   | Leu |
| Glu | Ala<br>1970 | Val | Ser | Gly | Leu   | Gln<br>1975 | Val | Pro   | Asn   | Cys | Cys<br>1980 | Glu | Pro   | Gly |
| Ile | Ala<br>1985 | Thr | Gly | Thr | Glu   | Arg<br>1990 | Asn | Phe   | Thr   | Ala | Arg<br>1995 | Val | Gln   | Arg |
| Gly | Ser<br>2000 | Arg | Val | Ala | Tyr   | Ala<br>2005 | Trp | Tyr   | Phe   | Ser | Leu<br>2010 | Gln | Lys   | Val |
| Gln | Gly<br>2015 | Asp | Ser | Leu | Val   | Ile<br>2020 | Leu | Ser   | Gly   | Arg | Asp<br>2025 | Val | Thr   | Tyr |
| Thr | Pro<br>2030 | Val | Ala | Ala | Gly   | Leu<br>2035 | Leu | Glu   | Ile   | Gln | Val<br>2040 | Arg | Ala   | Phe |
| Asn | Ala<br>2045 |     | Gly | Ser | Glu   | Asn<br>2050 | Arg | Thr   | Leu   | Val | Leu<br>2055 | Glu | Val   | Gln |
| Asp | Ala<br>2060 | Val | Gln | Tyr | Val   | Ala<br>2065 | Leu | Gln   | Ser   | Gly | Pro<br>2070 | Сув | Phe   | Thr |
| Asn | Arg<br>2075 |     | Ala | Gln |       | Glu<br>2080 | Ala | Ala   | Thr   | Ser | Pro<br>2085 | Ser | Pro   | Arg |
| Arg | Val<br>2090 |     | Tyr | His | Trp   | Asp<br>2095 |     | Gly   | Asp   | Gly | Ser<br>2100 | Pro | Gly   | Gln |
| Asp | Thr<br>2105 | -   | Glu | Pro | Arg   | Ala<br>2110 |     | His   | Ser   | Tyr | Leu<br>2115 | Arg | Pro   | Gly |
| Asp | Tyr<br>2120 | _   | Val | Gln | Val   | Asn<br>2125 | Ala | Ser   | Asn   | Leu | Val<br>2130 | Ser | Phe   | Phe |
| Val | Ala<br>2135 |     | Ala | Thr | Val   | Thr<br>2140 |     | Gln   | Val   | Leu | Ala<br>2145 |     | Arg   | Glu |
| Pro | Glu<br>2150 |     | Asp | Val | Val   | Leu<br>2155 | Pro | Leu   | Gln   | Val | Leu<br>2160 |     | Arg   | Arg |
| Ser | Gln<br>2165 | _   | Asn | Tyr | Leu   | Glu<br>2170 |     | His   | Val   | Asp | Leu<br>2175 |     | Asp   | Cys |
| Val | Thr<br>2180 | _   | Gln | Thr | Glu   | Tyr<br>2185 |     | Trp   | Glu   | Val | Tyr<br>2190 |     | Thr   | Ala |
| Ser | Cys<br>2195 |     | Arg | Pro | Gly   | Arg<br>2200 |     | Ala   | Arg   | Val | Ala<br>2205 |     | Pro   | Gly |
| Val | Asp<br>2210 |     | Ser | Arg | Pro   | Arg<br>2215 |     | Val   | Leu   | Pro | Arg<br>2220 |     | . Ala | Leu |
| Pro | Val<br>2225 |     | His | Tyr | Cys   | Phe<br>2230 |     | Phe   | Val   | Val | Ser<br>2235 |     | : Gly | Asp |
| Thr | Pro<br>2240 |     | Thr | Gln | . Ser | lle<br>2245 |     | . Ala | . Asn | Val | Thr<br>2250 |     | Ala   | Pro |

- Glu Arg Leu Val Pro Ile Ile Glu Gly Gly Ser Tyr Arg Val Trp 2255 2260 2265
- Ser Asp Thr Arg Asp Leu Val Leu Asp Gly Ser Glu Ser Tyr Asp 2270 2275 2280
- Pro Asn Leu Glu Asp Gly Asp Gln Thr Pro Leu Ser Phe His Trp 2285 2290 2295
- Ala Cys Val Ala Ser Thr Gln Arg Glu Ala Gly Gly Cys Ala Leu 2300 2305 2310
- Asn Phe Gly Pro Arg Gly Ser Ser Thr Val Thr Ile Pro Arg Glu 2315 2320 2325
- Arg Leu Ala Ala Gly Val Glu Tyr Thr Phe Ser Leu Thr Val Trp 2330 2335 2340
- Lys Ala Gly Arg Lys Glu Glu Ala Thr Asn Gln Thr Val Leu Ile 2345 2350 2355
- Arg Ser Gly Arg Val Pro Ile Val Ser Leu Glu Cys Val Ser Cys 2360 2365 2370
- Lys Ala Gln Ala Val Tyr Glu Val Ser Arg Ser Ser Tyr Val Tyr 2375 2380 2385
- Leu Glu Gly Arg Cys Leu Asn Cys Ser Ser Gly Ser Lys Arg Gly 2390 2395 2400
- Arg Trp Ala Ala Arg Thr Phe Ser Asn Lys Thr Leu Val Leu Asp 2405 2410 2415
- Glu Thr Thr Thr Ser Thr Gly Ser Ala Gly Met Arg Leu Val Leu 2420 2425 2430
- Arg Arg Gly Val Leu Arg Asp Gly Glu Gly Tyr Thr Phe Thr Leu 2435 2440 2445
- Thr Val Leu Gly Arg Ser Gly Glu Glu Glu Gly Cys Ala Ser Ile 2450 2460
- Arg Leu Ser Pro Asn Arg Pro Pro Leu Gly Gly Ser Cys Arg Leu 2465 2470 2475
- Phe Pro Leu Gly Ala Val His Ala Leu Thr Thr Lys Val His Phe 2480 2485 2490
- Glu Cys Thr Gly Trp His Asp Ala Glu Asp Ala Gly Ala Pro Leu 2495 2500 2505
- Val Tyr Ala Leu Leu Leu Arg Arg Cys Arg Gln Gly His Cys Glu 2510 2515 2520
- Glu Phe Cys Val Tyr Lys Gly Ser Leu Ser Ser Tyr Gly Ala Val 2525 2530 2535
- Leu Pro Pro Gly Phe Arg Pro His Phe Glu Val Gly Leu Ala Val

- Val Val Gln Asp Gln Leu Gly Ala Ala Val Val Ala Leu Asn Arg 2555 2560 2565
- Ser Leu Ala Ile Thr Leu Pro Glu Pro Asn Gly Ser Ala Thr Gly 2570 2580
- Leu Thr Val Trp Leu His Gly Leu Thr Ala Ser Val Leu Pro Gly 2585 2590 2595
- Leu Leu Arg Gln Ala Asp Pro Gln His Val Ile Glu Tyr Ser Leu 2600 2605 2610
- Ala Leu Val Thr Val Leu Asn Glu Tyr Glu Arg Ala Leu Asp Val 2615 2620 2625
- Ala Ala Glu Pro Lys His Glu Arg Gln His Arg Ala Gln Ile Arg 2630 2635 2640
- Lys Asn Ile Thr Glu Thr Leu Val Ser Leu Arg Val His Thr Val 2645 2650 2655
- Asp Asp Ile Gln Gln Ile Ala Ala Leu Ala Gln Cys Met Gly 2660 2665 2670
- Pro Ser Arg Glu Leu Val Cys Arg Ser Cys Leu Lys Gln Thr Leu 2675 2680 2685
- His Lys Leu Glu Ala Met Met Leu Ile Leu Gln Ala Glu Thr Thr 2690 2695 2700
- Ala Gly Thr Val Thr Pro Thr Ala Ile Gly Asp Ser Ile Leu Asn 2705 2710 2715
- Ile Thr Gly Asp Leu Ile His Leu Ala Ser Ser Asp Val Arg Ala 2720 2725 2730
- Pro Gln Pro Ser Glu Leu Gly Ala Glu Ser Pro Ser Arg Met Val 2735 2740 2745
- Ala Ser Gln Ala Tyr Asn Leu Thr Ser Ala Leu Met Arg Ile Leu 2750 2760
- Met Arg Ser Arg Val Leu Asn Glu Glu Pro Leu Thr Leu Ala Gly 2765 2770 2775
- Glu Glu Ile Val Ala Gln Gly Lys Arg Ser Asp Pro Arg Ser Leu 2780 2785 2790
- Leu Cys Tyr Gly Gly Ala Pro Gly Pro Gly Cys His Phe Ser Ile 2795 2800 2805
- Pro Glu Ala Phe Ser Gly Ala Leu Ala Asn Leu Ser Asp Val Val 2810 2815 2820
- Ile Ser Asn Tyr Thr Val Ser Thr Lys Val Ala Ser Met Ala Phe 2840 2845 2850
- Gln Thr Gln Ala Gly Ala Gln Ile Pro Ile Glu Arg Leu Ala Ser

Glu Arg Ala Ile Thr Val Lys Val Pro Asn Asn Ser Asp Trp Ala Ala Arg Gly His Arg Ser Ser Ala Asn Ser Ala Asn Ser Val Val Val Gln Pro Gln Ala Ser Val Gly Ala Val Val Thr Leu Asp Ser Ser Asn Pro Ala Ala Gly Leu His Leu Gln Leu Asn Tyr Thr Leu Leu Asp Gly His Tyr Leu Ser Glu Glu Pro Glu Pro Tyr Leu Ala Val Tyr Leu His Ser Glu Pro Arg Pro Asn Glu His Asn Cys Ser Ala Ser Arg Arg Ile Arg Pro Glu Ser Leu Gln Gly Ala Asp His Arg Pro Tyr Thr Phe Phe Ile Ser Pro Gly Ser Arg Asp Pro Ala Gly Ser Tyr His Leu Asn Leu Ser Ser His Phe Arg Trp Ser Ala Leu Gln Val Ser Val Gly Leu Tyr Thr Ser Leu Cys Gln Tyr Phe Ser Glu Glu Asp Met Val Trp Arg Thr Glu Gly Leu Leu Pro Leu Glu Glu Thr Ser Pro Arg Gln Ala Val Cys Leu Thr Arg His Leu Thr Ala Phe Gly Ala Ser Leu Phe Val Pro Pro Ser His Val Arg Phe Val Phe Pro Glu Pro Thr Ala Asp Val Asn Tyr Ile Val Met Leu Thr Cys Ala Val Cys Leu Val Thr Tyr Met Val Met Ala Ala Ile Leu His Lys Leu Asp Gln Leu Asp Ala Ser Arg Gly Arg Ala Ile Pro Phe Cys Gly Gln Arg Gly Arg Phe Lys Tyr Glu Ile Leu Val Lys Thr Gly Trp Gly Arg Gly Ser Gly Thr Thr Ala His Val Gly Ile Met Leu Tyr Gly Val Asp Ser Arg Ser Gly His Arg His Leu Asp Gly Asp Arg Ala Phe His Arg Asn Ser Leu Asp Ile Phe 

Arg Ile Ala Thr Pro His Ser Leu Gly Ser Val Trp Lys Ile Arg Val Trp His Asp Asn Lys Gly Leu Ser Pro Ala Trp Phe Leu Gln His Val Ile Val Arg Asp Leu Gln Thr Ala Arg Ser Ala Phe Phe Leu Val Asn Asp Trp Leu Ser Val Glu Thr Glu Ala Asn Gly Gly Leu Val Glu Lys Glu Val Leu Ala Ala Ser Asp Ala Ala Leu Leu Arg Phe Arg Arg Leu Leu Val Ala Glu Leu Gln Arg Gly Phe Phe Asp Lys His Ile Trp Leu Ser Ile Trp Asp Arg Pro Pro Arg Ser Arg Phe Thr Arg Ile Gln Arg Ala Thr Cys Cys Val Leu Leu Ile Cys Leu Phe Leu Gly Ala Asn Ala Val Trp Tyr Gly Ala Val Gly Asp Ser Ala Tyr Ser Thr Gly His Val Ser Arg Leu Ser Pro Leu Ser Val Asp Thr Val Ala Val Gly Leu Val Ser Ser Val Val Val Tyr Pro Val Tyr Leu Ala Ile Leu Phe Leu Phe Arg Met Ser Arg Ser Lys Val Ala Gly Ser Pro Ser Pro Thr Pro Ala Gly Gln Gln Val Leu Asp Ile Asp Ser Cys Leu Asp Ser Ser Val Leu Asp Ser Ser Phe Leu Thr Phe Ser Gly Leu His Ala Glu Gln Ala Phe Val 

Gly Gln Met Lys Ser Asp Leu Phe Leu Asp Asp Ser Lys Ser Leu Val Cys Trp Pro Ser Gly Glu Gly Thr Leu Ser Trp Pro Asp Leu Leu Ser Asp Pro Ser Ile Val Gly Ser Asn Leu Arg Gln Leu Ala Arg Gly Gln Ala Gly His Gly Leu Gly Pro Glu Glu Asp Gly Phe Ser Leu Ala Ser Pro Tyr Ser Pro Ala Lys Ser Phe Ser Ala Ser 

- Asp Glu Asp Leu Ile Gln Gln Val Leu Ala Glu Gly Val Ser Ser 3470 3475 3480
- Pro Ala Pro Thr Gln Asp Thr His Met Glu Thr Asp Leu Leu Ser 3485 3490 3495
- Ser Leu Ser Ser Thr Pro Gly Glu Lys Thr Glu Thr Leu Ala Leu 3500 3505 3510
- Gln Arg Leu Gly Glu Leu Gly Pro Pro Ser Pro Gly Leu Asn Trp 3515 3520 3525
- Glu Gln Pro Gln Ala Ala Arg Leu Ser Arg Thr Gly Leu Val Glu 3530 3540
- Gly Leu Arg Lys Arg Leu Leu Pro Ala Trp Cys Ala Ser Leu Ala 3545 3550 3555
- His Gly Leu Ser Leu Leu Leu Val Ala Val Ala Val Ala Val Ser 3560 3565 3570
- Gly Trp Val Gly Ala Ser Phe Pro Pro Gly Val Ser Val Ala Trp 3575 3580 3585
- Leu Leu Ser Ser Ser Ala Ser Phe Leu Ala Ser Phe Leu Gly Trp 3590 3595 3600
- Glu Pro Leu Lys Val Leu Leu Glu Ala Leu Tyr Phe Ser Leu Val 3605 3610 3615
- Ala Lys Arg Leu His Pro Asp Glu Asp Asp Thr Leu Val Glu Ser 3620 3625 3630
- Pro Ala Val Thr Pro Val Ser Ala Arg Val Pro Arg Val Arg Pro 3635 3640 3645
- Pro His Gly Phe Ala Leu Phe Leu Ala Lys Glu Glu Ala Arg Lys 3650 3660
- Val Lys Arg Leu His Gly Met Leu Arg Ser Leu Leu Val Tyr Met 3665 3670 3675
- Leu Phe Leu Leu Val Thr Leu Leu Ala Ser Tyr Gly Asp Ala Ser 3680 3685 3690
- Cys His Gly His Ala Tyr Arg Leu Gln Ser Ala Ile Lys Gln Glu 3695 3700 3705
- Leu His Ser Arg Ala Phe Leu Ala Ile Thr Arg Ser Glu Glu Leu 3710 3715 3720
- Trp Pro Trp Met Ala His Val Leu Leu Pro Tyr Val His Gly Asn 3725 3730 3735
- Gln Ser Ser Pro Glu Leu Gly Pro Pro Arg Leu Arg Gln Val Arg 3740 3745 3750
- Leu Gln Glu Ala Leu Tyr Pro Asp Pro Pro Gly Pro Arg Val His 3755 3760 3765
- Thr Cys Ser Ala Ala Gly Gly Phe Ser Thr Ser Asp Tyr Asp Val

|     | 3770        |     |     |       |     | 3775          |     |     |       |     | 3780        |     |     |     |
|-----|-------------|-----|-----|-------|-----|---------------|-----|-----|-------|-----|-------------|-----|-----|-----|
| Gly | Trp<br>3785 | Glu | Ser | Pro   | His | Asn<br>3790   | Gly | Ser | Gly   | Thr | Trp<br>3795 | Ala | Tyr | Ser |
| Ala | Pro<br>3800 | Asp | Leu | Leu   | Gly | Ala<br>3805   | Trp | Ser | Trp   | Gly | Ser<br>3810 | Cys | Ala | Val |
| Tyr | Asp<br>3815 | Ser | Gly | Gly   | Tyr | Val<br>3820   | Gln | Glu | Leu   | Gly | Leu<br>3825 | Ser | Leu | Glu |
| Glu | Ser<br>3830 | Arg | Asp | Arg   | Leu | Arg<br>3835   | Phe | Leu | Gln   | Leu | His<br>3840 |     | Trp | Leu |
| Asp | Asn<br>3845 | Arg | Ser | Arg   | Ala | Val<br>3850   | Phe | Leu | Glu   | Leu | Thr<br>3855 | Arg | Tyr | Ser |
| Pro | Ala<br>3860 | Val | Gly | Leu   | His | Ala<br>3865   | Ala | Val | Thr   | Leu | Arg<br>3870 | Leu | Glu | Phe |
| Pro | Ala<br>3875 | Ala | Gly | Arg   | Ala | Leu<br>3880   |     | Ala | Leu   | Ser | Val<br>3885 |     | Pro | Phe |
| Ala | Leu<br>3890 | Arg | Arg | Leu   | Ser | Ala<br>3895   | Gly | Leu | Ser   | Leu | Pro<br>3900 | Leu | Leu | Thr |
| Ser | Val<br>3905 |     | Leu | Leu   | Leu | Phe<br>3910   | Ala | Val | His   | Phe | Ala<br>3915 |     | Ala | Glu |
| Ala | Arg<br>3920 |     | Trp | His   | Arg | Glu<br>3925   |     | Arg | Trp   | Arg | Val<br>3930 |     | Arg | Leu |
| Gly | Ala<br>3935 |     | Ala | Arg   | Trp | Leu<br>3940   |     | Val | Ala   | Leu | Thr<br>3945 |     | Ala | Thr |
| Ala | Leu<br>3950 |     | Arg | Leu   | Ala | Gln<br>3955   |     | Gly | Ala   | Ala | Asp<br>3960 |     | Gln | Trp |
| Thr | Arg<br>3965 |     | Val | Arg   | Gly | Arg<br>3970   |     | Arg | Arg   | Phe | Thr<br>3975 |     | Phe | Asp |
| Gln | Val<br>3980 |     | His | Val   | Ser | Ser<br>3985   |     | Ala | Arg   | Gly | Leu<br>3990 |     | Ala | Ser |
| Leu | Leu<br>3995 |     | Leu | Leu   | Leu | Val<br>4000   |     | Ala | Ala   | Gln | His<br>4005 |     | Arg | Phe |
| Val | Arg<br>4010 |     | Trp | Ser   | Val | Phe<br>4015   |     | Lys | Thr   | Leu | Cys<br>4020 |     | Ala | Leu |
| Pro | Glu<br>4025 |     | Leu | Gly   | Val | Thr<br>4030   |     | Gly | Leu   | Val | Val<br>4035 |     | Gly | Val |
| Ala | Tyr<br>4040 |     | Gln | . Leu | Ala | Ile<br>4045   |     | Leu | . Val | Ser | Ser<br>4050 |     | Val | Asp |
| Ser | Leu<br>4055 |     | Ser | · Val | Ala | Gln<br>4060   |     | Leu | Leu   | Val | Leu<br>4065 |     | Pro | Gly |
| Thr | Gly<br>4070 |     | Ser | Thr   | Leu | . Cys<br>4075 |     | Ala | Glu   | Ser | Trp<br>4080 |     | Leu | Ser |

Pro Leu Leu Cys Val Gly Leu Trp Ala Leu Arg Leu Trp Gly Ala 4085 4090 4095

Leu Arg Leu Gly Ala Val Ile Leu Arg Trp Arg Tyr His Ala Leu 4100 4105 4110

Arg Gly Glu Leu Tyr Arg Pro Ala Trp Glu Pro Gln Asp Tyr Glu
4115 4120 4125

Met Val Glu Leu Phe Leu Arg Arg Leu Arg Leu Trp Met Gly Leu 4130 4135 4140

Ser Lys Val Lys Glu Phe Arg His Lys Val Arg Phe Glu Gly Met 4145 4150 4155

Glu Pro Leu Pro Ser Arg Ser Ser Arg Gly Ser Lys Val Ser Pro 4160 4165 4170

Asp Val Pro Pro Pro Ser Ala Gly Ser Asp Ala Ser His Pro Ser 4175 4180 4185

Thr Ser Ser Ser Gln Leu Asp Gly Leu Ser Val Ser Leu Gly Arg 4190 4195 4200

Leu Gly Thr Arg Cys Glu Pro Glu Pro Ser Arg Leu Gln Ala Val 4205 4210 4215

Phe Glu Ala Leu Leu Thr Gln Phe Asp Arg Leu Asn Gln Ala Thr 4220 4225 4230

Glu Asp Val Tyr Gln Leu Glu Gln Gln Leu His Ser Leu Gln Gly 4235 4240 4245

Arg Arg Ser Ser Arg Ala Pro Ala Gly Ser Ser Arg Gly Pro Ser 4250 4255 4260

Pro Gly Leu Arg Pro Ala Leu Pro Ser Arg Leu Ala Arg Ala Ser 4265 4270 4275

Arg Gly Val Asp Leu Ala Thr Gly Pro Ser Arg Thr Pro Leu Arg 4280 4285 4290

Ala Lys Asn Lys Val His Pro Ser Ser Thr 4295 4300

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<220>

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| Coucce         | acc goodcooc aagoac          |    |
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| .010           |                              |    |
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| 72137          | AIDITIOIAI BEQUENCE          |    |
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|                | PCR primer BPR4              |    |
|                | •                            |    |
| <400>          | 6                            |    |
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| 1000           | Total Principality           |    |
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|                | -gggg                        |    |
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| <213>         | Artificial sequence      |     |
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| 12237         | Tex primer ne,           |     |
| -400-         | 10                       |     |
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| gtcaac        | gtgg gcctccaagt          | 20  |
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